# 1. MedWatch Report of a case of 68 year old patient with Jaundice and Transaminase elevation on 10mg of Rosuvastatin D3560L0001/0310/01237

<b>TT</b> 7	Astr	aZen	eca Pharmaceuticais	Common F		Approved by FQA on 3/22/
MEDIAATOII	•			JF/O=1 n	02PE01036	
MEDYVAICH	<u></u>					
THE FDA'MEDICAL PRODUCTS REPORTING PROGR.	<u>AM</u>		Page 1 of 4			
A. Patient information			C. Suspect mo	dication	e l	FDA Use One
Patient identifier     Age at time of event;     Character	3. Sett 4. Weigh	*	1. Name (give labeled stren	gth & mfr/labels	r, if known)	
or 68 yrs		. Ibs	# ROSUVASTATI		•	
in confidence Date of birth;	⊠ male 91 Or	kgs				
B. Adverse event or product proble	n	. nys	2. Doss, frequency & route		1. 5	
	lem (a.g., defects/maifunc		# 10 mg daily		06/07	(if unknown, give duration) /2002 to 10/09/2002
2. Outcomes attributed to adverse event		(IONS)				72002 E8 10/09/2002
	•	- 1	#2 4. Diagnosis for use (indic		22	·
	nital anomaly d intervention to prevent	- 1	# HYPERCHOLEST			5. Event shated after use stopped or dose reduced
	ent impairment/damage		- arranchomas	PROPERTY		#1 yes no doesn't
hospitalization - initial or prolonged other:			R			so yea no doesn't
3. Date of 10/08/2002 4. Date of		$\dashv$	4. Lot#(if known) et NI	, i	date (if known)	#2 yes no doesn't
instanti	10/28/2002		et MI	- NI		8. Event responsed after reintreduction
5. Describe event or problem			#2	- 2		# yes no doesn't
15-DAY IND ALERT			9. NOC # - for product proble		m)	apply
			et NI	R		#2yes no doesn't
CORRECTED REPORT: THE CLOCK	CT10T N1==	- 1	10. Concornitant medical pro	ducts and the	apy dates (exclude	resiment of event)
HAS BEEN CHANGED TO 11-OCT-2	OUS START DATE G-4	- 1				
10 11 00111	002	ľ	Name: GLUCOPHAGE Name: CAPTOBETA 1	850 Dates	: NI to NI	
Clinical Event(s):			Name: ESCOR Dates	: NI to M	I .	
1 HEPATOPATHY			G. All manufact			
2 ICTERUS		- 1	1. Contact office - nemeledá	See (& mirror	são for devices)	2. Phone number
			Astrazeneca Pharm	aceutical		302 886 2127
A report has been received	from an		A Business Unit o	f Astraze	neca LP.	
investigator concerning a 68-	-year-old male	- 11	1800 Concord Pike Wilmington, DE 19	, P.O. Bo	z 15437,	(check all that apply)
patient who was enrolled in	the ORBITAL stud	tv		#30-343/		oreign
D3560L00001, an open, random	sed parallel	- 11				study
group study evaluating the en	fects of six					consumer
months rosuvastatin treatment	plus additions	11				health
compliance initiatives compar	ed to		4. Date received by manufactu			professional
rosuvastatin alone on long-te	rm *		11-OCT-2002	1.,	DA #	user facility
Relevant tests/laboratory data _ including dates	· · · · · · · · · · · · · · · · · · ·			IN	D #	company
			6. If IND, protocol II	Pl	^#	distributor
			D3560L00001	pr	e-1938 🔲 y	
			7. Type of report (check all that apply)		rc 🗆 y	1
			☐ 5-day 🛛 15-day			DE
			10-day periodic	- 1	verse event term(s)	
•		- 1 1		Нера	tocellular	damage, Jaundice
		- [ ]	☑ Initial ☐ follow-up #	NO8		
Other relevant history, including pressisting medical conditions pregnancy, smoking and alcohol use, hepatic/renal dysfunction	(e.g., allergies, race,	77	9. Mfr. report number			
			2002PK01036			
<b></b>			E. Initial reporter			
Concomitant Disease(s): DIABE	TES MELLITUS,		1. Name, eddress & phone #			
DIABETES MELLITUS TYPE II, PA	TTY LIVER, HEAR	F	, ,			
DISBASE, HYPERTENSION, PERIPH	ERAL OCCLUSIVE					
ARTERY DISEASE			•			1
Coherterio	<del></del>					1
Submission of a report doe admission that medical per	6 not constitute an		2. Health professional?	3. Occupation		Initial consider view
aistributor, manufacturer or	Droduct caused or		⊠ yes □ no	MEDICAL I	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	Initial reporter also sent report to PDA
completed to the event, literal completed on continua	tion pages.	L.	<u>_</u>	ABDICAL I	OCTOR	yes no unk
	,					

MED WATCH	A.1. Patient identifier	G.9. Mfr. report number 2002PK01036	
			Page 2 of 4

## B.5. Describe event or problem

[continuation:] disease-related costs in patients with an indication for statin treatment according to the Joint European Guidelines.

Medical history included diabetes mellitus type II, peripheral occlusive artery disease, hypertension, an unspecified heart disease and a fatty liver caused by diabetes. Concomitant medication consisted of metformin and glibenclamide for diabetes, captopril for hypertension, nilvadipine for heart disease and clopidogrel for peripheral artery disease.

The patient started rosuvastatin 10 mg daily on 07-Jun-2002. After 17 weeks and 5 days on study medication, on 08-0CT-2002, he developed icterus with brown discolouration of urine. On the next day he was hospitalised and study drug withdrawn. Metformin, captopril, nilvadipine and clopidogrel were also withdrawn. Hepatopathy of unknown cause, most likeley drug-induced was diagnosed. Sonography showed parenchymal liver damage but histology revealed normal liver tissue. Hepatitis B and C were excluded. No pathologic findings of other abdominal organs except for mild splenomegaly. The patient's condition improved and he was discharged on 21-Oct-02.

The investigator did not exclude a causal relationship to the study medication but stated that a proper evaluation must await the results of further investigation. He stated that a contributory role of concomitant medications cannot be ruled out. Serious criterion was hospitalisation Further information was requested.

Summary of follow-up received on 22-Oct-02:

- Hepatopathy of unknown cause, most likely drug-induced
- rosuvastatin was stopped on 09-Oct-02
- patient's condition improved
- metformin, captopril, nilvadipine and clopidogrel were stopped too

# Company Clinical Comment:

Jaundice and hepatocellular damage occurring in a subject with a history of fatty liver of diabetic etiology should probably not be considered related to study medication, especially when histology revealed normal liver tissue. However, given the temporal relationship between event and study medication, a contributory role of rosuvastatin cannot be ruled out completely. Co-medications captopril, nilvadipine and clopidogrel should also be considered as suspected drugs because liver disorders are labeled for these drugs.

### 

[continuation:] LAB 09-OCT-02: Hepatitis B and C was ruled out

SONOGRAPHY: parenchymal damage of liver

HISTOLOGY: normal liver tissue

-			Ref. to		
Lab Test/Comment Lab Value	Units	Date	Normal	Low	High
BLOOD SEDIMENTATI42/65	mm	10/08/2002			

MED WATO	CH		2002PK0	1036		
			L			Page 3 of 4
B.S. Relevant tests/laboratory	data .including dates					
[continuation:]	ASAT	91		10/09/2002	INCREASED	< 37
ASAT	17	10/15	5/2002	NORMAL	< 37	,
ALAT	223	10/09	/2002	INCREASED	< 65	,
ALAT	80	10/15	/2002	INCREASED	< 65	
GGT	942	10/09	/2002	INCREASED	< 55	
GGT	657	10/15	/2002	Incr <u>eased</u>	< 37	
АР	130	10/09,	/2002			
AP	150	10/15/	/2002			
TOTAL BILIRUBIN	2.1	10/09/	<b>/2002</b> ]	Increased	< 1	
TOTAL BILIRUBIN	0.7	10/15/	'2002 N	FORMAL	< 1	
WBC	11.5	10/09/	2002 I	NCREASED		

10/15/2002

< 1

WBC

HBS-AG

HBC-AK

HCV-AK

7.6

negative

negative

negative

•	A.1. Patient identifier	G.S. Mir. report number	
MED WATCH	; 1	2002PK01036	
	I		Page 4 of 4

3.6. Relevant tests/laboratory data \_\_\_\_\_including date:

[continuation:]

C.10. Concomitant medical products and therapy dates (exclude treatment of event)

[continuation:] Name: PLAVIX Dates: NI to NI

Name: AZUGLUCON Dates: NI continuing

G.3. Report source (other:)

Source

# 2. MedWatch Report of a case of 73 year old patient with Jaundice and Transaminase elevation on 10mg of Rosuvastatin D3560L0001/2265/09060

U.S. Department of Health and Human Services	AstraZe	neca Pharmaceuticais	Form Approved: ONC (in. 091 Phone Foreman Femores off report #	0-0291 Express: 04/30/03 FDA Facetrale Assessed on 91/11/
IVIEDVVATCH	1		2002PE01330	
The FDA Safety Infromation and Adverse Event Reporting Program				
		Page 1 of 7		
A. Patient information		C. Suspect me	dication(s)	FOA Vise On
1. Patient identifier 2. Age at time of event: 73 yrs	3. Seet 4. Weight	1. Name (give labeled stren)	gth & mir/lebeler, if known)	
or ———	femalethe	ROSUVASTATIN	<u> </u>	
in confidence Dute of taleth:	⊠ male 84 kgs	a a		<del></del>
B. Adverse event or product problem		2. Dose, frequency & route u	and 3 Thermout	ntes (if unknown, give duration)
1. Adverse event and/or Product proble	m (e.g., defects/malfunctions	an 10 mg daily	PO g 09/1	1/2002 to 12/03/2002
2. Outcomes attributed to adverse event (check all that apply)				
death	y tał anomaly	4. Diagnosis for use (indica	tion)	T
(moteuring) required	intervention to prevent	# HYPERCHOLEST	•	<ol> <li>Event shaled after use stopped or dose reduced</li> </ol>
perman	ent impairment/damage			#1 ☐ yes ☐ no ☐ doesn't
		& Lot# (if known)		yes no doesn't
3. Date of event 12/02/2002 4. Date of this report	05/07/2003	at NI	7. Exp. data (if known)	apply
5. Describe event or problem	03/07/2003		-	Event reeppeared after reintroduction
Section of property		9. NDC # - for product problem		#1 yes no doesn't
15-DAY IND ALERT		PI NI	ns only (if known) #2	apply
		I L		I I has I uo I oosesus
Clinical Event(s):		10. CONCERNMENT MEDICAL PROD	and therapy dates (exclu	de treatment of event)
1 ICTERUS	,	Name: DELIX		
2 CHOLECYSTITIS		Name: ASS "CT-ARE!	MRIMITTEL* Dates: (	1/77/2002 to 12/02/
	` *-	2002 •		30 22,02,
A report has been received fr	om study	G. All manufacti	irers	
investigator concerning a 73	year old male	Contact office - name/addre		2. Phone number
patient who was enrolled in t	he ORBITAL study	Astraženeca Pharms	ceuticals	302 886 2127
D3560L00001, an open, randomi	sed parallel	A Business Unit of 1800 Concord Pike,	Astraleneca LP,	3. Report source
group study evaluating the ef	fects of six	Wilmington, DE 198	150-5437	(check all that apply)  foreign
months rosuvastatin treatment	plus additional			study
compliance initiatives compar	ed to			literature
rosuvastatin alone on long-ter	rm disease-			consumer
related costs in patients with	an indication			⊠ health
for statin treatment according European Guidelines. *	; to the Joint	4. Data received by manufacture (moneyer)	(A)NDA#	professional
		22-APR-2003	IND# 56,385	user facility
Relevant testafaboratory data , including dates		6. If INO, protocal \$	PLA#	representative
		D3560L00001		distributor
		7. Type of report	pre-1938	ouner.
		(check all that apply)	OTC product	yos *
	İ	5-day 🛭 15-day		DE
		10-day periodic	8. Adverse overst term(	•
•		☐ Initial ☐ follow-up #.2	Jaundice MOS.	Cholecystitis NOS
7. Other retevant history, including premisting medical conditions	/a			1
pregnancy, smoking and alcohol use. hepatic/renal dysfunction.	(e.g., allergies, race, etc.)	9. Mr. report number		
	ļ	2002PR01330		
Concomitant Disease(s): CHOLEC	VOTOL ITHE LATA	E. Initial reporter		
CORONARY ARTERY DISEASE	unitalis,	1. Name & address	phone # 14	
	[ ]	`		
	] [			
Submission of a report does not	constitute an			
admission that medical personni	at ugar facility i		. Occupation	4. Initial reporter also
distributor, manufacturer or production of contributed to the event.		⊠yes ☐ no ,	GDICAL DOCTOR	sent report to FDA
* Item completed on continuati	on pages.	_ <del></del>		yes no Wunk

26	A.1. Patient identifier	G.S. Mir. report number	
MEDWATCH	1	2002PR01330	
		<u> </u>	Page 2 of 7

## B.5. Describe event or problem

[continuation:] The patient started study medication on 11-Sep-2002. Concomitant drugs were ramipril and acetylsalicylic acid. Medical history included cholecystolithiasis. Other relevant medical history consisted of hepatitis B during second world war. On 02-Dec-2002, eleven weeks and six days after commencing study medication, he experienced icterus. Total bilirubin (7.12 mg/dl), AP (303 U/1), GGT (77 U/1), ASAT (699 U/1) and ALAT (914 U/1) were increased. WBC was normal. A performed CT on 03-Dec-2002 revealed suspected carcinoma of pancreatic head, cholecystitis and splenomegaly. In further clinical course pancreatic cancer and acute hepatitis A, B and C were excluded. Hepatitis serology showed negative HBsAg but positive IgM anti-HBc. ERCP showed no stenosis of biliary ducts. The physicians considered perhaps some gallblader stones had passed but they could not exclude druginduced reactions. Further details were unknown at time of the report. Study drug was withdrawn and lab values were improving.

The reporter considered that as long as pancreatic cancer had not been confirmed the events were possibly related to study medication. Serious criterion was hospitalisation.

CT scan on 09-Dec-2002 ruled out pancreatic tumor. Liver transaminases are decreasing. Patient is scheduled for a cholecystectomy on 27-Jan-2003. Cholecystectomy was not performed because it was not certain that a gallstone was present. Investigational method was not stated at the time of this report. Lab values, specifically GGT (20 U/L), ASAT (11 U/L), ALAT (12 U/L) and total bilirubin (0.86 mg/dl) returned to normal. No further investigation regarding hepatitis serology was carried out.

# Company Clinical Comment

As with other HMG-CoA reductase inhibitors, increases in liver transaminases have been observed in a small number of subjects taking rosuvastatin. However, the elevation in transaminases observed in this subject does not appear to be related to study drug. The subject has a history of Hepatitis B during Second World War, but the presence of positive titers to IgM to anti-HB core and negative HB surface antigen suggests acute Hepatitis and not suggestive of previous infection. Therefore AstraZeneca disagrees with the investigators assessment of causality.

Summary of follow-up received on 10-Dec-02:

- Investigator considered event was not life-threatening
- lab values added

Summary of follow-up received on 16-Dec-02:

- pancreatic cancer and hepatitis A, B and C were excluded
- ERCP showed no stenosis of biliary ducts
- cholecystolithiasis added as concomitant disease added
- ramipril and acetylsalicylic acid added as concomitant drugs
- perhaps some gallbladder stones had passed

Summary of follow-up received on 17-Dec-02:

- lab values and patient's medical history added
- medical history included hepatitis B during second world war

Summary of follow-up received on 30-Jan-03: \*

•	A.1. Patient identifier	G.9. Mfr. report number	
MEDWATCH	:	2002PK01330	
			Page 3 of 7

## B.5. Describe event or problem

[continuation:] - hospital discharge letter, dated 20-Dec-02, received

- no evidence for a pancreatic tumor,
- diagnosis of mild intrahepatic cholestasis and a renal cyst left
- diagnosis of angiosclerosis of Aorta abdominalis
- patient is scheduled for a cholecystectomy on 27-Jan-03

Summary of follow-up information received on 22-Apr-2003:

- no evidence for gallstone, therefore cholecystectomy cancelled
- lab vaues for ASAT, ALAT, GGT, AP returned to normal
- no further investigation regarding hepatitis serology.
- narrative updated

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[CONTINUATION:] CT 04-DEC-02: CHOLECYSTITIS AND SUSPECTED CANCER HEAD OF PANCREAS. NO CONCREMENTS I GALLBLADDER, NORMAL BILE DUCTS, DUCTUS CHOLEDOCHUS DIFFICULT TO ASSESS. SPLENOMEGALY ABDOMINAL SONOGRAPHY 09-DEC-02: NO CHOLECYSTOLITHIASIS 09-DEC-02: CT SCAN SHOWED NO EVIDENCE FOR PANCREATIC TUMOR; MILD INTRAHEPATIC CHOLESTASIS; SOFT TISSUE DENSE STRUCTURE IN THE AREA OF THE HEPATIC PORTAL, POSSIBLE REGIONAL SWELLING OF LYMPH NOTO OR BILIARY DUCT; NO ENLARGEMENT OF ABDOMINAL LYMPH NODES; RENAL CYST LEFT; ANGIOSCLEROSIS OF AORTA ABDOMINALIS

Lab Test/Comment	Lab Value	Units	Date	Ref. to Normal	Low	High	
TOTAL BILIRUBIN	7.12	mg/dl	12/04/2002	Increased		< 1.1	
AP	303	U/1	12/04/2002	INCREASED		< 180	
GGT	77 ~	U/1	12/04/2002	INCREASED		< 28	
GPT	914	U/1	12/04/2002	INCREASED		< 24	
GOT	699	U/1	12/04/2002	INCREASED		< 18	
WBC	5100	/ul	12/04/2002	NORMAL	4000	9400	*

	A.1. Patient Identif	Rer	G.9. Mfr. 1	report number			
CH	 	· · · · · · · · · · · · · · · · · · ·	20029	K01330			Page 4 of 7
	including dates						
4.5	56	Mio/ul	12/04/2002	NORMAL	4.5	6.3	
14.	.7	g/dl	12/04/2002	NORMAL	′ <b>14</b>	18	
43		*	12/04/2002	NORMAL	38	52	
171	000	/ul	12/04/2002	NORMAL	150000	4400	00
195			12/06/2002				
113			12/07/2002				
59			12/10/2002				
59		• •	12/10/2002				
58			12/12/2002				
65			12/16/2002				
577			12/06/2002				
447			12/07/2002				
185			12/10/2002				
157			12/12/2002				
	CH  y data  1  4.9  14.9  14.9  59  58  65  577  447  185	y data including dates  1 4.56 14.7 43 171000 195 113 59 59 58 65 577 447	y data including dates  1 4.56 Mio/ul 14.7 g/dl 43 171000 /ul 195 113 59 59 58 65 577 447	Tydeta including dates  1 4.56 Mio/ul 12/04/2002 14.7 g/dl 12/04/2002 171000 /ul 12/04/2002 195 12/06/2002 113 12/07/2002 59 12/10/2002 59 12/10/2002 59 12/10/2002 59 12/10/2002 59 12/10/2002 59 12/10/2002	CH   2002PK01330  y data	CH   2002PK01330  y data	CH   2002PK01330  77 data

) ( YYZ	A.1. Patient Identifier	G.9. Mfr. report number	
MEDWATCH	1	2002PK01330	
			Page 5 of 7

B.G. Relevant testa-faborator	y data including dates		
[continuation:		137	12/16/2002
GGT	62	12/06/2002	
GGT	59	12/07/2002	,
GGT	53	12/10/2002	
GGT	62	12/12/2002	
AP .	267	12/06/2002	
АР	260	12/07/2002	
AP	230	12/10/2002	
AP	266	12/12/2002	
AP	237	12/16/2002	
TOTAL BILIRUBIN	11.0	12/06/2002	
TOTAL BILIRUBIN	11.8	12/07/2002	
TOTAL BILIRUBIN	7.6	12/10/2002	
TOTAL BILIRUBIN	8.2	12/12/2002	
TOTAL BILIRUBIN	6.0	12/16/2002	

Ti control of the con	A.1. Patient identifier	G.9. Mfr. report number	
MedWatch		2002PK01330	
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							_
B.G. Relevant testalsborator	V <b>data</b> including dates						
	-		12/03/200	2			
ANTI-HEPBC IGM PRESENT	positive		12/03/200	2	,		
HEP A IGG-ANTII PRESENT	BODnegative		12/03/2002	2			
CONJUGATED BILI	CRU3.1	mg/dl	12/16/2002	1			
WBC	3.6	T∎d/ul	02/12/2003	DECREASED	4.0	9.4	
BRYTHROCYTES	4.59	MIO/ul	02/12/2003	NORMAL	4.5	6.3	
HAEMOGLOBIN	15.4	g/dl	.02/12/2003	NORMAL	14	18	
HCV	102	£1,		Increased	78	98	
мсн	34	pg		INCREASED	26	32	
мснс	33	g/dl	02/12/2003	NORMAL	32	36	
THROMBOCYTES	157	Tsd/ul	02/12/2003	NORMAL	150	440	
TOTAL BILIRUBIN	0.86	mg/dl	02/12/2003	NORMAL		1.1	
AP	138	U/L	02/12/2003	NORMAL		180	
ganona gt	20	U/L	02/12/2003	NORMAL		29	
ASAT	11	U/L	02/12/2003	NORMAL		18	•
	Continuation: HBSAG ABSENT  ANTI-HEPBC IGM PRESENT  HEP A IGG-ANTII PRESENT  CONJUGATED BILI  WBC  ERYTHROCYTES  HAEMOGLOBIN  MCV  MCH  MCHC  THROMBOCYTES	HESAG negative ABSENT  ANTI-HEPBC IGM positive PRESENT  HEP A IGG-ANTIBODNegative PRESENT  CONJUGATED BILIRU3.1  WBC 3.6  ERYTHROCYTES 4.59  HAEMOGLOBIN 15.4  MCV 102  MCH 34  MCHC 33  THROMBOCYTES 157  TOTAL BILIRUBIN 0.86  AP 138  GAMMA GT 20	HESAG negative ABSENT  ANTI-HEPBC IGN positive PRESENT  HEP A IGG-ANTIBODnegative PRESENT  CONJUGATED BILIRU3.1 mg/d1  WBC 3.6 Tsd/u1  ERYTHROCYTES 4.59 MIO/u1  HAEMOGLOBIN 15.4 g/d1  MCV 102 fl  MCH 34 Pg  MCHC 33 g/d1  THROMBOCYTES 157 Tsd/u1  TOTAL BILIRUBIN 0.86 mg/d1  AP 138 U/L  GANNA GT 20 U/L	Continuation:   HBSAG   negative   12/03/200   ABSENT			CONTINUATION:   RESAG   REGATIVE   12/03/2002

	<b>MW</b>	A.1. Patient identifier	G.P. Mfr. report number		
L	MEDWATCH		2002PK01330		ĺ
				Page 7 of 7	

B.S. Relevant testallaboratory data incl.

[continuation:]

ALAT

12

U/L

02/12/2003 NORMAL

24

C.19. Concomitant medical products and therapy dates (exclude treatment of event)

[continuation:] Name: POTABA Dates: 09/77/2002 to 12/02/2002

G.3. Report source (other:)

Source

AstraZeneca Pharmaceuticals A Business Unit of AstraZeneca LP, 1800 Concord Pike, P.O. Box 15437, Wilmington, DE 19850-5437

Mfr. Rep. #: 2002PK01330

Date: 07-MAY-2003

LISTING OF PRIOR SAFETY REPORTS
SUBMITTED TO IND #

ADVERSE EVENT: Cholecystitis NOS

(all preferred and included coded terms)

 Manufacturer Report #
 FDA Submission Date
 Protocol Number
 Country of Origin

 2001UW06827
 24-OCT-2001
 4522IL/0034
 UNITED STATES

 2001UW08219
 26-OCT-2001
 4522IL/0034
 UNITED STATES

 2002PK01330
 20-DEC-2002
 D3560L00001
 GERMANY

ADVERSE EVENT: Jaundice NOS

(all preferred and included coded terms)

 Manufacturer Report #
 FDA Submission Date
 Protocol Number
 Country of Origin

 2002PK01036 2002PK01330
 29-OCT-2002
 D3560L00001
 GERMANY

 2002PK01330
 20-DEC-2002
 D3560L00001
 GERMANY

# 3. MedWatch Report of a case of Rhabdomyolysis on 10mg of Rosuvastatin 2003SE02255

U.S. Department of Health and Human Services  AstraZe	neca Pharmaceuticals  From Appropriate ONB No. 0010-0281 Express: 04-02603  From Express From Front Section FDA Forestella Appropriate Statistics  20038202255
The FDA Safety Inframetica and	UF Chat report #
The PDA Safety Infromation and Adverse Event Reporting Program	Page 1 of 7
A. Patient information	C. Suspect medication()
1. Patient identifier 2. Age at time of event: 3. Sex 4. Weight	C. Suspect medication(s)  1. Name (give labeled strungth & mirrisoter, if known)
or tos tos	
in confidence of births male 80 h	
B. Adverse event or product problem	
Adverse event and/or Product problem (e.g., defects/maffunctions)	territoria for facilitativa (in un accistant, gave duration)
2. Outcomes attributed to advance event	of 11/26/2002 to 04/14/2003
(check all that apply) disability	R
death congenital anomaly	4. Diagnosis for use (indication) S. Event stated after use stopped
iffe-threatening	et XI or deservations or deservations of does not does no
hospitalization - initial or prolonged other:	25 Sphy
3. Date of 4. Date of	6. Lat # (N known) 7. Exp. date (N known) 42 yes no doesn't
overst 04/20/2003 this report 05/30/2003	91 NY 90 NY 8. Event respected offer
5. Describe event or problem	minimoduciles
2 224 225 225	9. NDC 9 - for product probleme only (if fanour)
7-DAY IND ALERT	#1 MI #2 #2 yee no doesn't
234.1. 3. 5	10. Concomitant medical products and therapy dates (exclude treatment of event)
Clinical Event(s):	
1 ACUTE RENAL FAILURE	Name: METFORAL Dates: 11/??/2002 to 04/21/2003
2 CONCA	Name: TRIATEC Dates: 11/??/2002 to 04/21/2003
3 SEPTIC SHOCK	Name: LASIX Dates: 04/10/2003 to 04/21/2003 *
4 URINARY INFECTION	G. All manufacturers
• •	Contact effice - nameladdress (& miring site for devices)     Plane number
A report has been received from an	Astraleneca Pharmaceuticals 302 886 2127 A Business Unit of Astraleneca LP,
investigator regarding a 75-year-old female	1800 Concord Pike, P.O. Box 15437,
who was enrolled in study GISSI- HF with	Wilmington, DE 19850-5437
rosuvastatin versus placebo.	⊠ study
Madday 2 by the state of the st	☐ literature
Medical history included diabetes mellitus	consumer
type II (decompensated), cardiomyopathy,	health
peripheral neuropathy with pains in the legs,	4. Date received by manufacturer 5. professional frontiery (A)NDA #
chronic atrial fibrillation and congestive *	16-MAY-2003 IND † user facility company
Relevant testelaboratory data , including dates	6. If ND, protocol If PLA II representative
	G105 distributor
	7 Type of mark
	(check all that apply)
_	5-day 15-day 17
	E. Adverse event termics)
•	Initial   follow-up # 1   shock, Urinary tract infection
	NOS
Other retreant history, including president generalized conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepstic/renal dysfunction, etc.)	9. Mr. report number
	20038802255
	E. Initial reporter
Concomitant Disease(s): CARDIOMYOPATHY,	1. Name & address phone # Ni
CHRONIC ATRIAL FIBRILLATION, CONGESTIVE HEART	
FAILURE, PERIPHERAL NEUROPATHY, TYPE II	
DECOMPANSATED DIABETES	(*
Cultural and A and	
Submission of a report does not constitute an admission that medical personnel, user facility,	2. Health professional? 3. Occupation 4. Initial reporter also
admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.	yes no MEDICAL DOCTOR sent report to FDA unk
	, '   ∟ yes ∟ no ∠ unk /

l	A1. Fellent identifier	G.9. Mir. report number	
MEDWATCH		20038802255	
			Page 2 of 7

## B.S. Describe event or another

[continuation:] heart failure. Concomitant medication included ramipril, metformin hydrochloride, warfarin, furosemide, allopurinol and insulin human injection/isophane.

The patient was randomized to rosuvastatin on 26-Nov-2002. The study medication was stopped on 14-Apr-2003 because of clinical deterioration (worsening of heart failure). She was admitted to the GISSI-HF centre under the care of the investigator for congestive heart failure on 15-April-2003. The patient was asthenic with nausea and diarrhea since discharge on 18-April-2003. On 20-April-2003, she was taken to the Emergency Unit of another hospital and was transferred immediately to the Mephrology ward because of acute renal failure. Lab tests were performed and measured, WBC 25,000, Na 152, K 5.8: BUN 183: Creatinine 8.7: CK 10383 to 21632. A cerebral "computed axial tomography" showed no findings. The following day she went into a come with hypotension, acidosis and anuria and was transferred to an intensive care unit. The patient underwent mechanical ventilation, hemodialysis and received treatment with Imipenem because of suspected septic shock. She improved and was awake in the afternoon on 22-Apr-2003. On 28-Apr-2003 she was transferred to the Nephrology ward with lab test measuring: BUM 26; Creatinine 3 and CK 424. On 12-May-2003, patient was treated with linesolid 600 mg BID and metronidazole 500 mg TID for urinary infection with Enterococco faecium. Fluconasolo and Cephalosporin were added to patient therapy with discovery of Pseudomonas and Candida tropicalis. he renal function continued to improve with serum creatinine 1.8 mg and CPR 226U/1 on 16-May-2003 hen she was transferred to the GISSI Heart Failure Center with the following diagnoses "Acute renal failure secondary to a very probable septic shock in a diabetic with chronic atrial fibrillation, urinary infection due to Enterococco Faecium, Pseudomonas Aeruginosa and Candida tropicalis, sacral Ulcer, trophyc ulcer in the legs".

After reviewing the discharge summary from 21-Apr-2003 to 16-May-2003, the investigator reported acute renal failure, coma, septic shock, urinary infection, Enterococco Faecium as serious adverse events and assessed all of them not to be causally related to rosuvastatin. Coma, septic shock and renal failure were considered by the investigator to be life threatening. The investigator considered that the hemodynamic conditions of the septic shock might explain the rise in CK levels, which are back within normal ranges now.

Summary of follow-up information received by AstraZeneca 07-May-2003 and 08-May-2003: Lab values and further information on concomitant medications, the hospitalizations and the diagnosis of rhabdomyolysis.

Summary of follow-up information received by AstraZeneca 16-May-2003: The patient has been transferred from the nephrology ward to the internal medicine ward. Reason for acute renal failure was provided.

Summary of follow-up information received by AstraZeneca 19-May-2003: Hospitalization summary, additional laboratory results, the deletion of rhabdomyolysis as a serious adverse event and the attribution of raised CPK to Septic Shock, the addition of Coma as a serious adverse event and the change in causality assessment.

Summary of follow-up information received by AstraZeneca 26-May-2003: Examinations done during the \*

1	A1. Pullent identifier	G.S. Mir. report number	
MEDWATCH		20038202255	
L			Page 3 of 7

## B.S. Describe event or problem

[continuation:] first hospitalization together with clarification of laboratory findings. Two additional serious adverse events of septic shock and urinary infection were added.

Summary of follow-up information received by AstraZeneca 28-May-2003: Summary of second hospitalization with additional laboratory findings.

Company Clinical Comment: Acute renal failure and come occurred 6 and 7 days after stopping rosuvastatin. The investigator considered these events to be related to the septic shock and not rosuvastatin. The events of acute renal failure, come, septic shock and urinary infection were all considered not causally related to rosuvastatin by the investigator.

# B.G. Relevant testalisboratory data \_\_\_\_\_including dates

[continuation:] Cerebral assial tomography: negative. No signs or symptoms of mesenteric or cardiac ischemia.

16-May-2003: Negative blood culture.

15th to 18th April 2003: Thoraxicic x-ray, ECG and lab examinations.

b Test/Comment	Lab Value	Units	Date	Ref. to Normal	Low	High
CREATININE	0.8	• •	11/??/2002			
ĸ	3.79		11/??/2002			
GLUCOSE	208		11/??/2002			
BLOOD GLUCOSE	138	MG/DL	04/15/2003			
CREATININE	3.8	MG/DL	04/15/2003			
NA	152 ~		04/21/2003			
ĸ	5.8		04/21/2003			
BUN	183		04/21/2003			

ř	A1. Patient Identifier	G.S. Mir. report number	T
MedWatch		20038102255	
	<u> </u>	<u> </u>	Page 4 of 7

8.4 Relevant testalationstory of [continuation:]		8.7		04/21/2003
ск	10383		04/21/2003	
ск	21632		04/21/2003	
BUN	26		04/28/2003	
CREATININE	3		04/28/2003	
СЖ	424		04/28/2003	
OPERATURE	37.5	CELCIUS	05/16/2003	
WHITE CELLS	13600	/mmc	05/16/2003	
нв	11.6	GR%	05/16/2003	
PLATELETS	251000	/mmc	05/16/2003	
N	100	MG%	05/16/2003	
Creatinine	1.8	MG*	05/16/2003	
AST	20	U/L	05/16/2003	
ALT	7	U/L	05/16/2003	
D <sub>1</sub>	140	mEq/L	05/16/2003	

			A1. Patient Identifier	?		G.S. Mfr. report number	
	MEDWATC	H	·			20038102255	Page 5 of 7
	8.6. Relevant testafaboratory of [continuation:]	<b>144</b> 3 . (	, including dates	mEq/L	05/1	L6/2003	
		94		-		,	
	CL			mEq/L		16/2003	
	CA.	8.6	•	MG%	05/1	.6/2003	
	INR	1.2	19		05/1	6/2003	
	PTT	33.	9	SEC	05/1	6/2003	
<b>4</b>	FIBRINOGENO	666	i	MG/DL	05/1	6/2003	<u>-</u> -
	CPK	226	· <b>~</b>	U/L	05/1	6/2003	
	PH	7.5	5		05/16	6/2003	
	PCO2	97			05/16	5/2003	
	ECO3	38.	4		05/16	5/2003	
	SATURATION 02	98		•	05/16	5/2003	
	HEMOGLOBIN	10.	3		04/21	./2003	
	WHITE CELLS	2500			04/21	./2003	
	GLYCENIA	140			04/21	/2003	
	LDH	322			04/21	/2003	•

	A1. Patient Identifier	G.S. Mir. report number	
MEDWATCH	•	20038#02255	
	<u> </u>		Page 6 of 7

B.A. Ralovant testafabors	8.6. Relevant testafuboratory data including dates									
[continuation	1:]									
LDR	535			04/21/2003						
BILIRUBIN	0.6			04/21/2003						
SGOT	172			04/21/2003						
SGOT	316			04/21/2003						
SGPT	58			04/21/2003						
SGPT	90			~04/21/2003						
PH	7.31		* *	04/21/2003						
PACO2	24			04/21/2003						
PAO2	73			04/21/2003						
BE	13			04/21/2003						
HCO3	11.7			04/21/2003						
LACTATE	16	~		04/21/2003						
PT	11		•	04/21/2003						
PTT	49		SECONDS	04/21/2003						

#Y	A1. Patlant Mendiller	G.S. MY, report number	
MEDWATCH	1	2003 <b>520</b> 2255	
		<u> </u>	Page 7 of 7

B.S. Reinvert testalisheratory data inchetion data

[continuation:]

C.18. Concentant medical products—and therapy dates (exclude treatment of event)

[continuation:] Name: ZYLORIC Dates: 04/15/2003 to 04/21/2003

Name: HUMULIN 30/70 Dates: 11/7?/2002 to 04/21/2003
Name: WARFARIN Dates: ??/??/2001 to 04/21/2003

G.1. Report source (other:)

Source

# 4. MedWatch Report of a case of 46 year old patient with Renal Failure on 80mg of Rosuvastatin 0065/0044/0014

MEDWATCH	•	neca Pharmaceuticals	Option Facentie  Air report 8  20020W01954  JF/Det report 8	Assessment to FDA on 32
HE FDA MEDICAL PRODUCTS REPORTING PROGR.	AM	Page 1 of 5		
A. Patient information				fDA Use O
Patient identifier	3. Sex 4. Weight	C. Suspect medic	ation(s)	
of event: 46 yrs	53	Name (give labeled strength &	mfr/labeler, if known)	
or Date		PI ROSUVASTATIN		
of birth:	male 62.7 kgs	SZ ZITHROMAN Z-PAC	:R	
<ul> <li>B. Adverse event or product problet</li> </ul>	n	2. Does, frequency & route used		. If water
	em (e.g., defects/malfunctions)	et 80 mg QD PO		(if unknown, give duration) 2001 to 01/26/2002
2. Outcomes attributed to adverse event	(org., octobramandricpons,	11		2001 08 01/26/2002
(check all that apply) disabili	•	#2 500 mg QD PO	#2 01/23/	2002 to 01/23/2002
(mortey/yr)	nital anomaly	4. Diagnosis for use (indication)		5. Event shated after use stooms
Derma	d intervention to prevent nent impairment/damage	#1 HYPERCHOLESTERO	LECIA	or dose reduced
hospitalization - initial or prolonged other:	ion imperimentating	2 PEVER		#1 yes no Ocesn'
		6. Lot # (if known)	7. Exp. date (if known)	#2 yes no doesn't
svent 02/02/2002 4. Oate of this report	1 03/01/2002	at NI	# MI	apoly
5. Describe event or problem				8. Event reappeared after reintroduction
- Second event or problem	7	772	N2 MI	#1 yes no doesn't
15-DAY IND ALERT		9. NDC # - for product problems or	nly (# known)	apply
		NI NI	AZ MI	#2 yes no ⊠ doesn't
Clinical Event(s):		10. Concomitant medical products	and therapy dates (exclude	realment of event)
1	1			•
1 ACUTE RENAL FAILURE		Name: ASPIRIN "BAYER	* Dates: 07/30/20	1 continuing
		Name: GUAIFEMESIN Da	tes: 01/23/2002 to	01/27/2002
A report was received from a	study	L		
investigator concerning a 46	-year-old	G. All manufactures	rs	
Hispanic female subject who	was enrolled in A	Contact office - name/address	(& mfring site for devices)	2. Phone number
Six-week, Open label, Doge-co	MOATISON Study	Astrazeneca Pharmaceu	uticals	302 886 2127
to Evaluate the Safety and E	ficecy of	A Business Unit of As	StraZeneca LD.	
Rosuvastatin versus Atorvast	ation	1800 Concord Pike, P.	.O. Box 15437,	3. Report source (check all that apply)
Cerivastatin, Pravastatin, as	d alman	Wilmington, DE 19850-	-5437	foreign
Subjects with Hypercholester	d Simvastatin in			⊠ study
0065).	plemia (ZD4522IL/			[] Interature
00037.				consumer
<b>-1</b> . • • · · · · ·				⊠ health
The subject had a medical his		4. Date received by manufacturer	5.	professional
hypercholesterolemia, hyperte	nsion, *	14-FEB-2002	(A)NDA #	user facility
6. Relevant tests/laboratory data , including dates	·		IND#	_ Company
		6. If IND, protocol #	PLA#	representative
	1	4522IL/0065	pre-1938  ves	distributor
		7. Type of report	OTC C	other:
		(check all that apply)	product yes	1
		5-day 🛭 15-day		
		10-day periodic	8. Adverse event term(s)	
•	11	☑ Initial ☐ follow-up #	RENAL PAILURE AC	TUTE
	1.1	- Hitter I TOHOW-up #		
<ol><li>Other relevant history, including preexisting medical conditions pregnancy, smoking and alcohol use, hepatic/renal dysfunction.</li></ol>	(e.g., allergies, race,	9. Mfr. report number	7	
	, etc. ,	2002UW01954	1	
Concomitant Disease(s): ABDOM	INAL AORTIC	E. Initial reporter		
STENOSIS, ACUTE BOWEL OBSTRUCT	TION. ANEMYA	1. Name, address & phone #		
CATARACTS, COUGH, DYSPNEA ON 1	VPRETON			
PERIPHERAL VASCULAR DISEASE, 1	MERTION,			. 1
THE THEOLOGICAL DISEASE,	WALE *			
Submission of a report does	not constitute an	2. Health professional? 3. Oc		
admission that medical personal distributor, manufacturer or		yes no	cupation 4,	Initial reporter also sent report to FDA
contributed to the event.	Product caused of	MED:	ICAL DOCTOR	yes no unk
item completed on continua	tion pages.		- · ·	

MED WATCH	A.1. Patient Identifier	G.9. Mr. report number 20020W01954		
· · · · · · · · · · · · · · · · · · ·			Page 3 of 5	

## 8.5. Describe event or problem

[continuation:] right-sided renal artery stenosis caused by external compressions relieved surgically (1979), claudication secondary to abdominal acrtic stenosis for which Palmaz stenting was performed (1993), small-bowel obstruction secondary to volvulus (1992), chronic anemia, subclavian artery disease, rare headaches, peripheral vascular disease, trace mitral regurgitation, dyspnea on exertion, cough, anemia, and cataracts.

The subject was randomized to study drug on 26-Dec-2001. Her concomitant medications were Atacand 16 mg daily (from 05-Apr-1999 to 02-Feb-2002) and aspirin 81 mg daily. Her baseline creatinine was 0.7 mg/dL. On 11-Jan-2002 (Day 16) the subject had protocol scheduled laboratory tests that revealed a CK of 45 U/L, an ALT of 19 U/L, AST of 18 U/LL and a creatinine of 1.1 mg/dL. On 23-Jan-2002 (Day 28), the subject presented to her primary care physician complaining of coryza and "flu" symptoms. The physician prescribed guaifenesin and azithromycin on 23-Jan-2002, which the subject took until 25-Jan-2002 and 27-Jan-2002, respectively. On 26-Jan-2002 (Day 31) the subject discontinued ZD4522. Her trial participation terminated 28-Jan-2002 (Day 33). The subject was seen at the investigative site on 28-Jan-2002. At that time she complained of nausea, anorexia and fatigue. Laboratory testing on that date revealed a CK of 41 U/L, ALT of 15 U/L, AST of 23 U/L, and creatinine of 11.0 mg/dL. The subject was hospitalized on 02-Feb-2002 with acute renal failure. The investigator's initial impression was that the renal insufficiency was related, not to study drug, but to Atacand.

tal signs and no acute findings. The creatinine on admission was 13.7 mg/dL (local lab normal range 0.5-1.5 mg/dL). Urinalysis on admission (local lab) showed 30 mg/dL protein (normal = neg), small blood (normal = neg), many bacteria, 10-15 WBC/hpf (normal 0-3), 15/20 RBC/hpf (normal 0-5), 1-3 coarse granular and 5-8 hyaline casts/hpf. Urine culture showed mixed organisms. A duplex abdominal/renal scan performed on 04-Feb-2002 revealed no stenosis of either renal artery and a hypoechoic cortical matrix bilaterally with multiple small cystic masses in both kidneys. In the hospital, she responded rapidly to intravenous fluids and bicarbonate. Dialysis was not required. The subject was discharged from the hospital on 08-Feb-2002. Her creatinine at that time was 3.8 mg/dL (local lab).

After discussion with the nephrologist regarding the timing of the azithromycin administration, the investigator considered the event no longer related to Atacand but to azithromycin. The study drug could not be ruled out as a contributor to the event. On 13-Feb-2002, the patient had a creatinine of 2.2 mg/dl. The patient was scheduled for an outpatient visit to the nephrologist on 20-Feb-2002. At this visit a serum creatinine level would be obtained.

Follow up information received 14-Feb-2002 included updates to causality assessments, laboratory data, medical history, suspect drugs, and therapy dates.

## Company Comment:

Acute renal failure is a labeled adverse event for azithromycin. Treatment with angiotensin receptor blockers (eg., candesartan, losartan) has also been associated with acute renal failure. Due to their temporal relationship, a possible role between rosuvastatin and the reported event cannot be tally excluded. \*

MED WATCH	A.1. Patient Identifier	G.9. Mfr. report number	
MED VVAICH	I	20020W01954	·
			Page 4 of 5

[continuation:]

# 8.6. Relevant tests/laboratory data ,including dates

[continuation:] 02-FEB-2002: URINALYSIS SHOWED 30 MG/DL PROTEIN (NORMAL = NEG), SMALL BLOOD (NORMAL = NEG), MANY BACTERIA, 10-15 WBC/HPF (NORMAL =0-3), 15/20 RBC/HPF (NORMAL =0-5), 1-3 COARSE GRANULAR AND 5-8 HYALINE CASTS/HPF. URINE CULTURE SHOWED MIXED ORGANISMS. 04-FEB-2002: DUPLEX ABDOMINAL/RENAL SCAN: REVEALED NO STENOSIS OF EITHER ARTERY AND A HYPOECHOIC

CORTICAL MATRIX BILATERALLY WITH MULTIPLE SMALL CYSTIC MASSES IN BOTH KIDNEYS.

Lab Test/Commen	it Lab Value	Units	Date	Ref. to	Low	High
CREATININE BASELINE	0.7	MG/DL				
СК	45	U/L	01/11/2002			
ALT	19	U/L	01/11/2002			
AST	18	U/LL	01/11/2002			
CREATININE	1.1	MG/DL	01/11/2002			
CK	41	U/L	02/28/2002			
ALT	15	U/L	02/28/2002			
AST	23	U/L	02/28/2002			
CREATININE	11.0	MG/DL	02/28/2002			
CREAININE	13.7	MG/DL	02/02/2002	. 0	.5	1.5
CREATININE	3.8	MG/DL	02/08/2002			

MED WATCH	A.1. Patient Identifier	G.9. Mfr. report number 20020W01954	
			Page 5 of 5

B.S. Relevant tests/taboratory data .including dates

[continuation:]

CREATININE

2.2

MG/DL

02/13/2002

8.7. Other relevant history, including preexisting medical conditions (e.g., atlergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

[continuation:] HEADACHES, RENAL ARTERY STENOSIS, SUBCLAVIAN ARTERY DISEASE, TRACE MITRAL REGURGITATION

Race: HISPANIC

AstraZeneca Pharmaceuticals
A Business Unit of AstraZeneca LP,
1800 Concord Pike, P.O. Box 15437,
Wilmington, DE 19850-5437

Mfr. Rep. #: 2002UW01954

Date: 01-MAR-2002

LISTING OF PRIOR SAFETY REPORTS
SUBMITTED TO IND #

**ADVERSE EVENT: RENAL FAILURE ACUTE** 

(all preferred and included coded terms)

 Manufacturer Report #
 FDA Submission Date
 Protocol Number
 Country of Origin

 2000UW03538
 21-DEC-2001
 4522IL/0025
 UNITED STATES

 2001UW00740
 22-MAY-2001
 4522IL/0034
 UNITED STATES

 2001UW15902
 30-JAN-2002
 4522IL/0065
 UNITED STATES

# 5. MedWatch Report of a case of 70 year old patient with Renal Failure on 80mg of Rosuvastatin 0065/0026/0049

MEDWATCH	AstraZe	neca Pharmaceuticals	Orman Ference Mir report 8 2001UN15902 JF/Crist report 8	Asserted by FDA on 3/2/
E FDA MEDICAL PRODUCTS REPORTING PROGRAM		Page 1 of 5		
A. Patient information  1. Patient identifier 2. Age at time 1	Sex 4. Weight	C. Suspect medi  1. Name (give labeled strength	ication(s)	FDA Use Onv
of event: 70 yrs	Female 169 ibs		i & mtr/abeler, if known)	
•	Or Or		·	
B. Adverse event or product problem	kgs	2. Doss, frequency & route use	·	
	(e.g., defects/maifunctions		hands for heat an	(d' unknown, give duration)
2. Outcomes attributed to adverse event	(a.g., derects/mailunctions	11	# 11/14/	2001 to 11/29/2001
- Consequency		4 01	<u>R</u>	
death congenital	anomaly itervention to prevent	4. Olegnosis for use (indication of HYPERCHOLESTES		5. Event abated after use stopped or dose reduced
Dermanen	impairment/damage		TOLERIA	#1 yes no doesn't
hospitalization - initial or prolonged other:		12		apply
1. Date of 9 arent 11/29/2001 4. Date of	0. (0. (0.0)	& Lot#(if known)	7. Exp. date (if known)	apply
event 11/29/2001 this report (middle/yr)  5. Describe event or problem	01/29/2002		an MI	Event reeppeared after reintroduction
a. Describe event or problem		9. NOC 8 - for product problems	82	#1 yes no doesn't
7-DAY IND ALERT		9. NDC#- for product problems	only (if known)	apply apply
		10 Concentrat modes and		Traceout Incident
Clinical Event(s):		10. Concomitant medical produc	and therapy dates (exclude	Irealment of event)
1 RENAL FAILURE		Name: DIOVAN "NOVAR	TIS" Dates: 01/01/	2000
		Mame: VIOXX Dates:	01/01/2000 continu	ina
A report was received from an	investigator	Name: NORVASC Dates	: 03/03/2001 conti	nuing •
regarding a 70 year-old, female	patient who	G. All manufactur	ers	
entered a 6-week, Open label, 1	Dose-comparison	1. Contact office - name/address		2. Phone number
Study to Evaluate the Safety as	nd Efficacy of	AstraZeneca Pharmac	euticals	302 886 2127
Rosuvastatin versus Atorvastati	ln,	A Business Unit of 1800 Concord Pike,	AstraZeneca LP,	3. Report source
Cerivastatin, Pravastatin, and	Simvastatin in	Wilmington, DE 1985	P.O. BOX 15437, 0-5437	(check all that apply)
Patients with Hypercholesterole	mia (ZD4522IL/			foreign Study
0065). The patient began therap	y with			literature
rosuvastatin 80 mg po daily on	14-Nov-2001			consumer
and subsequently experienced re	mal failure.			⊠ health
The patient had a medical histo	ory of	4. Date received by manufacturer (morasys)	5. (A)NDA#	professional
osteoporosis, hypertension, ben	ign breast *	24-JAN-2002	IND#	User facility
6. Relevant testallaboratory data . including dates		6. If IND, protocal #		_ company representative
	Ì	4522IL/0065	PLA#	distributor
		7. Type of report	pre-1938	other:
		(check all that apply)	OTC product yes	
		5-day 15-day		
		10-day periodic	8. Adverse event term(s)	
•		☐ Initial ☐ follow-up #.2	RENAL FAILURE A	CUTE
7. Other relevant bissess and it				
<ol> <li>Other relevant history, including pressisting medical conditions pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.</li> </ol>	(e.g., allergies, race,	9. Mfr. report number		
<del>-</del>		2001UW15902		
Concomitant Disease(s): BENIGN 1		E. Initial reporter		
DEPRESSION, HYPERTENSION, INFLA	OKEAST CYST,	1. Hame, address & phone #		
OSTEOPOROSIS, SUPPLEMENT	MARTION,			1
, boll bearing	İ			
Submission of a report does no	ot constitute an			
admission that medical person	nel, user facility.		Occupation 4.	Initial reporter also
distributor, manufacturer or pro	educt caused or	⊠ yes ☐ no Ha	DICAL DOCTOR	sent report to FDA
contributed to the event.	pages.			∟ yes □ no ⊠ unik

	A.1. Patient Identifier	G.9. Mfr. report number	<del></del>
/IED WATCH		2001UW15902	
		<u> </u>	Page 2 of 5

## B.5. Describe event or problem

[continuation:] cyst, obesity, and depression. Concomitant medications included Diovan (valsartan), Vioxx (rofecoxib), Norvasc (amlodipine), selenium, and Paxil (paroxetine). At the scheduled visit prior to randomization to study drug (November 7, 2001), her creatinine was 1.0 mg/dl, ALT was 10 U/L, AST was 15 U/L, and ALP was 54 U/L. Her CPK at randomization was 51 U/L, ALT was 9 U/L, and AST was 13 U/L. On November 28, 2001 (Day 15), the CPK was 69 U/L, creatinine was 2.3 mg/dl, ALT was 8 U/L, AST was 13 U/L, and ALP was 75 U/L.

On November 29, 2001 (Day 16), the patient reported to the emergency room complaining of generalized achiness, right-sided abdominal pain, nausea, and vomiting. Gallstones were detected and the patient was treated (treatment unknown at this time) and sent home. Her creatinine was subsequently found to have been 3.0 mg/dl. On 29-Nov-2001, the investigator requested that the patient permanently stop study medication. On December 3, 2001 (Day 20), the patient returned to the hospital and was admitted with a diagnosis of renal failure of unknown etiology. The patient's creatinine was 8.0 mg/dl. The CPK was 137 U/L (ULN = 130 U/L) and the myoglobin was 195 mg/dl (ULN = 51 mg/dl). The treating physician reported that the liver function tests, lipase, amylase, and white blood counts were normal. Viral hepatitis was ruled out. The physician also reported that the patient had no fever and urinalysis was unremarkable. An abdominal ultrasound was positive for 3 gallstones. An abdominal CT scan and HIDA scan were negative. The patient was immediately scheduled for dialysis.

4-Dec-2001, the patient's creatinine was 9.4 mg/dl. On 6-Dec-2001, the physician reported that the etiology remained unknown and the patient was dialyzed on 4-Dec-2001 and 5-Dec-2001. On 6-Dec-2001, the patient was also scheduled to receive dialysis. On 6-Dec-2001, the physician reported that the creatinine was < 4.0 mg/dl, the CPK was 108 U/L, and myoglobin was 150 mg/dl. The patient was stable and not considered in critical condition, however, the abdominal pain persisted. As of December 10, 2001 the creatinine was 5.0 mg/dl and 4.8 mg/dl and the patient was receiving hemodialysis every other day. The abdominal symptoms had improved with the use of Reglan (metoclopramide). On December 10, 2001, a CT-guided renal biopsy revealed acute tubular necrosis of unknown etiology. On an unknown date, the patient was discharged from the hospital. At the time of this report, the patient was recovering. The patient had been receiving dialysis three times a week and was diagnosed with anemia. The patient was then decreased to two times a week for dialysis and was being treated with Epoetin and vitamin supplements for her anemia.

The investigator assessed the event to be severe in intensity, life threatening, and possibly related to rosuvastatin in view of the temporal sequence of the event and study drug administration.

Company comment: Concomitant angiotensin II antagonist (valsartan) and Cox 2 inhibitor (rofecoxib) therapy may have contributed to the event, as acute renal failure is listed for both of these drugs. Hopsital records are pending. It is difficult to assess the causal role of rosuvastatin until complete information is obtained. This is the first report of renal failure that is not associated with myopathy.

Follow-up received 20-Dec-2001 added kidney biospy results and additional creatinine value of 4.8 mg/ . Ouctome updated to recovering from not yet recovered and on an unknown date, the patient was \*

	A.1. Patient identifier	G.9. Mfr. report number	
_ 1ED WATCH	; ;	2001UW15902	
	<u> </u>		Page 3 of 5

# B.5. Describe event or problem

[continuation:] discharged from the hospital.

Follow-up received 10-Jan-2002, reported the patient had been receiving dialysis three times a week and remained weak. She was diagnosed with anemia.

Follow-up received 24-Jan-2002 reported the patient was reduced to dialysis two times a week. She was being treated with Epoetin and vitamin supplements for her anemia.

# B.6. Relevant tests/laboratory data including dates

[continuation:] LIVER FUNCTION TESTS, LIPASE, AMYLASE, AND WHITE BLOOD COUNTS WERE NORMAL AND VIRAL HEPATITIS WAS RULED OUT.

ABDOMINAL ULTRASOUND WAS POSITIVE FOR THREE GALLSTONES.

ABDOMINAL CT SCAN AND HIDASCAN WERE NEGATIVE.

10-DEC-2001: CT GUIDED RENAL BIOPSY SHOWED ACUTE TUBULAR NECROSIS OF UNKNOWN ETIOLOGY.

Lab Test/Commen	t Lab Value	Units	Date	Ref. to Normal	Low	High
CREATININE	1.0	MG/DL	11/07/2001		0.7	1.4
JT.	10	U/L	11/07/2001		5	25
AST	15	U/L	11/07/2001		8	22
ALP	54	U/L	11/07/2001		32	72
CPK	51	U/L	11/14/2001		0	120
ALT	9	U/L	11/14/2001		5	25
AST	13	U/L	11/14/2001		8	22
CPK	69	U/L	11/28/2001		0	120
CREATININE *	2.3	MG/DL	11/28/2001	•	0.7	1.4

		ent identifier	G.9. Mfr. report numbe			
IED WAT	CH		2001UW15902	-		
						Page 4 of 5
B.4. Relevant testafeborse [continuation		g dates				
ALT	8	U/L	11/28/2001	5	25	
AST	13	U/L	11/28/2001	<b>.</b>	22	
ALP	75	U/L	11/28/2001	32	72	
CREATININE	3.0	MG/DL	11/29/2001	0.7	1.4	
CREATININE	8.0	MG/DL	12/03/2001	0.7	1.4	
СРК	137	U/L	12/03/2001	10	130	,
"OGLOBIN	195	NG/DL	12/03/2001	19	51	
CREATININE	9.4	MG/DL	12/04/2001	0.7	1.4	
CREATININE	<4.0	MG/DL	12/06/2001			
CPK	108	U/L	12/06/2001			
MYOGLOBIN	150	NG/DL	12/06/2001			
CREATININE	5.0	MG/DL	12/10/2001			
CREATININE	4.8	MG/DL	12/10/2001			

	A.1. Patient Identifier	G.9. Mfr. report number	
IED WATCH		2001UN15902	
	I		Page 5 of 5

C.16. Concomitant medical products and therapy dates (exclude treatment of event)

[continuation:] Name: SELENIUM Dates: 01/01/1995 continuing

Name: PAXIL Dates: 03/03/2001 continuing

AstraZeneca Pharmaceuticals
A Business Unit of AstraZeneca LP,
1800 Concord Pike, P.O. Box 15437,
Wilmington, DE 19850-5437

Mfr. Rep. #: 2001UW15902

Date: 29-JAN-2002

LISTING OF PRIOR SAFETY REPORTS
SUBMITTED TO IND #

ADVERSE EVENT: RENAL FAILURE ACUTE

(all preferred and included coded terms)

 Manufacturer Report #
 FDA Submission Date
 Protocol Number
 Country of Origin

 2000UW03538
 21-DEC-2001
 4522IL/0025
 UNITED STATES

 2001UW00740
 22-MAY-2001
 4522IL/0034
 UNITED STATES

 2001UW15902
 31-DEC-2001
 4522IL/0065
 UNITED STATES

# 6. MedWatch Report of a case of 69 year old patient with Interstitial Nephritis on 80mg of Rosuvastatin 0034/0316/0025

	<b>TT</b> -			AstraZe	neca Pt	armaceuticals		Outnote Fac			Asserted by FDA on 3/72
MED	$\lambda \lambda \lambda / \lambda T$								18208724		
MEL	YYAI	UH						JF/Cliet repa	et 6		
THE FDA MEDICA	L PRODUCTS REPORTI	NG PROGRAM	4		Page 1	of 13					
<ol><li>A. Patient in</li></ol>	nformation				C.	Suspect n					FDA Use On
Patient identifier	2. Age at time of event:		3. Sex	4. Weight		ame (give labeled st	rength & n	nton(s)	( known)		
	or69	yrs	lemale	NI Ibs	#1	ROSUVASTAT					
in confidence	Oute of birth:	ļ	Male male	NI or		ROSUVASTAT					
B. Adverse	event or product	problem		kgs		oee, frequency & rou	_				
1. Adverse ever				ts/malfunctions		80 mg dail					inknown, give duration)
<ol><li>Outcomes attributed (check all that apply)</li></ol>	In advance and			- Individual	1 ]	<del></del>		[			0 to 11/30/2001
death	,	disability	al anomaly		4 04	NI Ignoris for use (inc	4		#2 12/24		l to 04/15/2002
life-threatenic	(moldaylyr)	required	intervention to	Dravent	) an	HYPERCHOLE		AEWTA		5.00	vert abated after use stopped r dose reduced
	n - initial or prolonged	permane	nt impairment/	damage	-					<b>#</b> [	yes na doesn't
	in - imital or prolonged	L other:			82	HYPERCHOLES				J <sub>22</sub> T	yes no doesn't
3. Date of event 1.0	/24/2001	4. Date of this report	06/17/	2002	1 (	WI		7. Exp.del 91 NI	le (if known)		apply
5. Describe event or pro		Sample of the Party of the Part		2002	<del></del> -	NI .				A E	rent reeppeared after introduction
					-	C#- for product pro		NI NI		<b>↓</b> # [	yes ☐ no⊠ doesn't
15-DAY I	ND ALERT				61 N			42 NI (# Known)	•	1.7	apply
					10. Co	-					yes no ⊠ doesn't   spoly
	Event(s):			•		ncomitant medical p	roducts	and therap	y dales (exclud	a ireatm	ent of event)
	TITIAL NEPHRIT				Наше	: DISPRIM D	ates:	77/77/1	1995 to M		
A repor	t has been rec	eived co	ncerning	r a 69-	Name	: FLANCAZINE					
year-old	male who was	enrolled	i in an c	pen		: DETADINE			TINGS DIV	<b>/</b>	
label, m	ulticentre ext	ension t	rial to	222022	G.	All manufac	turers	š			
(recurred	-term safety a	nd effic	acy of Z	D4522		tact office - neme/ed			for devices)		2. Phone number
homerche	tatin) in subj	ects wit	:h		A Bu	aZeneca Phar siness Unit	Maceut	ticals		ļ	302 886 2127
romivest	lesterolemia.	After tr	eatment	with	1800	Concord Pik	o. P.C	. Box	Ca LP, 15437.		3. Report source
Was obser	atin 80 mg for rved on routin	r year	and 6 mo	nths it	Wilms	ington, DB 1	9850-5	437	,		(check all that apply)  foreign
had devel	loped proteinu	e scuay	Visit th	at he	i						⊠ study
sediment	associated with	rie with	act146	ĺ							literature
creatinin	ne. A nephrolog	71 m	e in ser	4	1						consumer
the patie	ent have a rene	al hione		a that	4 Date :	eceived by manufact		-			health professional
later the	patient was !	nospital	ised for	*bo *	()*********	P <sup>1</sup> P <sup>1</sup>		S. (A)NDA	#		user facility
6. Relevent tests/aborato			101	CHO -	05-	JUM-2002		IND	,		company
				1	E. WIND	, protocol #		PLA	·		representative
				- 11	45221	L/0034		pre-1			distributor
				f i	7. Type	of report		OTC	W	F	other:
				11	_	all that apply)		produ	ici 🗆 ye	15 j	ZA
				11	_	ny 🖾 15-day		S. Advert	te ovent term(s)		<u> </u>
•				- []		ay Deriodic			TIS INTE		TAL
					Initia	il 🛭 follow-up	*4				
7. Other relevant history, is	ncluding premisting medica	i conditions	(e.g., allergies,	race.	9. Mfr. re	port number	$\dashv$				
programmy, arranging	d alcohol use, hepatic/renal	dysfunction, str	c.)	.	200151		1				
							اـــــا				
Concomita	nt Disease(s):	BACK AC	HE, LEG			litial reporte	r				
ULCERS, ST	TASIS LEG ULCE	RS			1400 370,						
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CDΔ	Submission of a re-	port does n	ot constitute	an	7	professional?	T				
	admission that med distributor, manufa	cturer or or	aduct course			no no	3. Occu		I	initial r	eporter also
men Facemen of	contributed to the e	vent.					MEDIC	TAL DOC	TOR	_	es 🗆 no 🛛 unk
			· payes.								

	A.1. Patient identifier	G.9. Mir. report number	
MED WATCH		20015E08724	
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## B.5. Describe event or problem

[continuation:] biopsy.

Follow-up information received 29-NOV-2001:

The patient was diagnosed with chronic interstitial nephritis, cause unknown. The medical history includes hypercholesterolaemia, stasis leg ulcers since '87, treated with flamazine, Betadine, topical steroids and intramuscular penicillin for over 10 years. The last Bicillin injection was in July 2001. Patient also has a history of backache and was hospitalized with inflammation of kidneys at age eight years. Patient recovered without known sequelae.

He has a history of heavy alcohol use but stopped totally in 1983. Concurrent medications are rosuvastatin 80 mg daily, 0.5 disprin daily for the past 18 months, intermittent intramuscular penicillin for chronic leg ulcers, and occasional paracetamol for pain. During the 6-week dietary lead- in period of the trial, prior to rosuvastatin exposure, there were two abnormal urinalyses; the first showed no protein but did show active sediment, the second showed 1+ protein and some bacteria, but no active sediment. Baseline serum creatinine in November 1999 was 84 mmol/1 (1.1 mg/dl). The subject was seen for a routine study visit in December 2000, at which time his serum creatinine had risen to 141 mmol/l (1.6 mg/dl). Urinanalysis was not performed. Creatinine was measured again at a study visit in October 2001, at which time the subject reported no symptoms but the serum creatinine was still elevated at 141 mmol/l and urinanalysis showed 3-protein with active sediment. LDL-C was 61 mg/dl from a baseline of 282 mg/dl. He was referred to a nephrologist who evaluated the subject in early November 2001. The subject remained asymptomatic and reported no edema. He had a ormal blood pressure and unremarkable physical exam. Local lab results were as follows: urinalysis revealed 1+ protein, 3+ blood, and numerous granular casts with moderate numbers of renal tubular cells. Complete blood count was unremarkable; ESR 31 mm/hour; Electrolytes, glucose, total protein, and albumin were normal; urea 10 mmol/1, creatinine 161 umol/1, glucose 3.9 mmol/1, total protein 80 g/l, albumin 44 g/l, total bilirubin 36 umol/l, conjugated bilirubin 10 umol/l. ALT 69 units/litre, alkaline phosphate 124 units/litre, creatinine kinase 238 units/litre. (Conventional units: urea 28 mg/dl, creatinine 1.8 mg/dl, glucose 70 mg/dl, total protein 8 gm/dl, albumin 4.4 gm/dl, total bilirubin 2.1 mg/dl, conjugated bilirubin 0.6 gm/dl). Baseline total bilirubin was elevated at 29 umol/1 (1.7 mg/dl). HbsAg negative; Hepatitis C antibody negative; ANF negative. Serum protein electrophoresis revealed no paraproteins and a normal albumin.

Uncorrected creatinine clearance was 42 ml/min. Baseline creatinine clearance was 61 ml/min. Daily protein excretion was 1.6 g/day, urea 388 mmol/day, sodium 171 mmol/day, potassium 68 mmol/day. Repeat serum creatinine on 20-Nov-2001 was 140 mmol/1 (1.6 mg/dl) and the urea 6.2 mmol/1 (17mg/dl). Renal biopsy performed on 20-Nov-2001 revealed features of chronic tubulo-interstitial nephritis with moderate increase in fibrous tissue and occasional inflammatory cells in the interstitium. These features were suggestive of a chronic process, present for many months and resulting in gradual collagen deposition within the interstitium, rather than an acute process. The nephrologist was not sure of the cause of the chronic interstitial nephritis and felt that it was remotely possible that rosuvastatin therapy may be responsible. Rosuvastatin was stopped 2001-Nov-30. Rosuvastatin was restarted on December 24 2001 at which stage proteinuria disappeared. There was only slight trace of blood and no casts. Plasma creatinine was 113 mmol/1, urea 6.4 mmol and 24 hour protein 80 mg. Urine samples were collected on December 26 and 29 2001, January 2 and 5 2002. On all these samples showed no detectable blood, protein or casts. Urine sample from January 16 was cloudy and with innumerable casts of all varieties. Sami quantitative tests showed 1+ protein and 2+ blood. Nephrologic consult of January 18 reported patient used two tablets of paracetamol 4 days prior to and one tablet 10 +

	A.1. Patient identifier	G.9. Mfr. report number	
MED WATCH	•	20018808724	
			Page 3 of 13

## 8.5. Describe event or problem

[continuation:] days prior to hospital visit for mild headache. There were no associated symptoms suggesting urinary tract infection or features of any other systemic disorder. The patient had also taken his routine half a disprin. Clinical examination revealed no abnormalities. Urine microscopy confirmed the previous findings. 24 hour protein excretion was 600 mg, plasma creatinine 119 mmol/l and urea 6.9 mmol/l. The patient continued with rosuvastatin for another week. The patient had a paracetamol challenge test. Four days after the challenge with paracetamol, cast numbers appeared to have increased. Urinary blood and protein was the same. Patient was continued on rosuvastatin. The patient was seen again on April 10. Ten days prior to the consultation the patient had a brief period of diarrhoea but was otherwise entirely asymptomatic and clinically well. The patient had not taken any drugs other than his statin and disprin. Urinanalysis revealed the presence of large number of casts, 3+ blood and 2+ protein. Urea was 6.7mmol/l, creatinine 120 mmol/l and 24 hour urine protein 1 300 mg. Rosuvastatin was stopped April 15 2002.

Nephrologist's report:

The nephrologist saw the patient on 27-May-2002 at which time all symptoms had totally resolved. Laboratory tests confirmed the absence of significant proteinuria on the last two occasions. 20-May-2002: Protein/ creatinine ratio 13.1 (equivalent to 110 mg protein per 24 hours). 27-May-2002: Protein/ creatinine ratio 16.4 (equivalent to 159 mg protein per 24 hours). Other chemistry: Sodium 137 mmol/1, potassium 3.9 mmol/1, potassium 3.9 mmol/1, urea 5.5 mmol/1, creatinine 108 mmol/1, AST 258, ALT 20, CPK 115, Hb 13.7, MCV 82, WCC 6.9, platelets 360, ESR 17. reatinine clearence 57 ml/min (corrected).

the conclusion was that the patient has lost all his urine abnormalities for a period of six weeks whilst of rosuvastatin therapy. Therapy with another statin at an equivalent dose to rosuvastatin was considered acceptable with very careful urine examination for at least six weeks.

Follow-up information 2001-Dec-14: Stop-date for rosuvastatin (study drug) was received. Several blood test results received, added on the lab. page.

Follow up information received 31 Jan 2002: Reporter confirmed that a causal relationship is possible with the event and study drug.

Summary of follow-up information received on 30-Apr-2002: Progress report from Nephrologist.

8-MAY-2002: Corrected report: Information was added (to the "Summary of follow-up information" in the end of narrative) concerning the content in follow-up information received on 30-Apr-2002.

14-MAY-2002: Corrected report. Information about dechallenge and rechallenge, start and stop date for suspect drug. Correction made in narrative concerning LDL (lipids) values.

16-MAY-2002: Corrected report. More detailed information from the original "Progress report" received on 30-Apr-2002, regarding investigations by nephrologist has been added to the narrative. Company Clinical Comment was changed.

16-MAY-2002: Rechallenge dose and clarification of dates.

Summary of follow-up information received on 5-Jun-2002: Nephrologist's report, see section "nephrologist's report above.

Company Clinical Comment: Renal papillary necrosis may result from chronic acetaminophen use, particularly when dosage is greater than recommended and when combined with aspirin. Patient was on Dispirin according to a previous list of concomitant medications and in this update, patient was taking acetaminophen. Dosage and duration were not provided. The nephrologist stated that proteinuria observed by 16 January 2002 might have been due to paracetamol (acetaminophen). However, the nephrologist tried both paracetamol and rosuvastatin during the same period in the rechallenge, \*

	A.1. Patient Identifier	G.9. Mir. report number	
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	<del></del>		Page 4 of 13

## B.5. Describe event or problem

[continuation:] making causality assessment very difficult. Due to the temporal relationship, and quasi positive rechallenge information, a possible role between rosuvastatin and the reported event cannot be excluded.

8.6. Relevant testa/aboratory datancluding dates [Continuation:]										
ab Test/Comment		Units	Date	Ref. to Normal	Low	High				
нз	12.5	g/dl				*				
HABMATOCRIT	0.37		. ·							
WCC	6 400									
PLATELETS	326									
ESR	31	MM/HOUR								
HBSAG	NEGATIVE									
HEPATITIS C ANTIE	HEPATITIS C ANTIBNEGATIVE									
anf	NEGATIVE	-								

## AstraZeneca Pharmacanticale

1	A.1. Patient identifier	G.9. Mfr. report number	
MED WATCH		20015808724	
			Page 5 of 13

•							
8.6. Relevant testa/leboratory	data .including dates						
[continuation:]							
SODIUM	142	MMOL/L					
POTASSIUM	4	MMOL/L			,		
UREA	10	1507 /r					
	20	MMOL/L					
CREATININE	161	UMOL/L					
GLUCOSE	3.9	MMOL/L					
TOTAL PROTEIN	80	G/L					
***************************************	00	G/L					
BUMIN	44	G/L	•				
TOTAL BILIRUBIN	36	UMOL/L					
CONJUGATED BILIR	II1 0	UMOL/L					
DIDIN	010	OMOL/L					
ALT	69	UNITS/L					
ALKALINE PHOSPHA	T124	UNITS/L					
CREATININE KINASI	<b>2</b> 220						
THE REAL PROPERTY.	9239	UNITS/L					
WBC	5.4 ~	K/cu mma	04/26/2000	NORMAT.	4.8	10.0	
			,		2.0	10.8	
RBC	5.32	M/cu mma	04/26/2000	NORMAL	4.20	5.40	
	-						
HGB	14 0	/ 50					
	14.8	gma/đĽ	04/26/2000	NORMAL	F 12.0	F 16.0	•

XX/	A.1. Patient Ide	ntiller	G.9. Mfr.	report number			
MED WATO	CH		2001s	E08724			
			<u>-</u> -				Page 6 of 13
O.A. Determent to a dist							
6.6. Relevant tests/aboratory		1					
	•						
HCT	45.9	*	04/26/2006	0	36.0	46.0	
мсн	27.8	pg	04/26/2000	,	27.0	31.0	
мснс	32.3 L	gmm/dL	04/26/2000	) DECREASED	33.0	33.7	
RDW	13.6	*	04/26/2000	NORMAL	11.5	14.5	
PLATELET COUNT	330	K/cu mm	04/26/2000	NORMAL	150	450	
METAMYELOCYTES	0	•	04/26/2000	NORMAL	0	0	- -
_AND NEUTROPHIL	BS0	*	04/26/2000	NOR <b>KA</b> L	0	11	-
SEGMENTED NEUTRO	DP66	*	04/26/2000		36	66	
LYMPHOCYTES	27	*	04/26/2000	NORMAL	24	44	
ATYPICAL LYMPHOC	<b>.</b> Y0	*	04/26/2000	NORMAL	0	0	
MONOCYTES	3	*	04/26/2000	NORMAL	0	11	
EOSINOPHILES	3 ~	*	04/26/2000	NORMAL	0	7	
BASOPHILES	1 .	*	04/26/2000	NORMAL	0	3	
SG (URINANALYSIS	1.020		04/26/2000	NORMAL	1.002	1.035	

A.1. Patien	t Identifier	G.9. Mfr. report r	Number .	1			
MED WATCH		200132087	24		_		
				<u>L</u>	P	age 7 of 13	
B.6. Relevant testafaboratory data including o							
[continuation:] PH (URINA)	NALYSIS) 6.0		04/26/2000 N	ORMAL.	5.0	8.0	
COLOUR (URINANALYYELLOW		04/26/2000					
APPEARANCE (URINACLEAR		04/26/2000	•				
PROTEIN (URINANALNEG	mg/dL	04/26/2000					
SLUCOSE (URINANANEG	mg/dL	04/26/2000					
ETONES (URINANANEG	mg/dL	04/26/2000					•
BILIRUBIN URINANANEG		04/26/2000					
LOOD URINANALYSNEG	• •	04/26/2000					
RBC (URINANALYSIOCC	нр г	04/26/2000	NONE	OCC/1	-5		
WBC (URINANALYSI1-5	HPF	04/26/2000	None	OCC/1	- 5		
ACTERIA (URINANAPRESENT H		04/26/2000	ABSENT				
YALINE CASTS (UR????	LPF	04/26/2000	none				
NELY GRANULAR C????	LPF	04/26/2000	NONE				
ORPH CRYSTALS (NONE	· LPP	04/26/2000	NONE				
EATININE (SERUM1.1	mg/dL	NOR	<b>MAL</b> 0.7	1.4			

			A.1. Patient identifier	G.S. Mir.	report number		<del></del>	
1 <u>M</u>	IED WA	TCH	<u> </u>		3E08724	<u>.</u>		Page 8 of 13
(co	biovani betalabori ontinuation 'AL BILIRUM	a:}	including dates	04/26/2000	0	0.10	1.10	
SGP	T (ALT)	20	mU/mL	04/26/2000	) NORMAL	5	25	
SGO:	r (ast)	20	mU/mI.	04/26/2000	NORMAL	8	22	
CPK		83	mU/mL	04/26/2000	NORMAL	0	120	
FP G	LUCOSE	94	mg/dL	04/26/2000	NORMAL	60	115	
TOTA	L CHOLESTI	ROL355	H mg/dL	04/26/2000	INCREASED	125	200	
RIG	LYCERIDER	(LI110	mg/dL	04/26/2000	NORMAL	45	200	
HDL	(LIPIDS)	51	mg/dL	04/26/2000	NORMAL	35	60	<u>-</u>
LDL	(LIPIDS)	282	H ng/dL	04/26/2000	INCREASED	50	160	ē
SGPT	(ALT)	19	mU/mL	05/12/2000	NORMAL	5	25	
SGOT	(AST)	20	mU/mL	05/12/2000	NORMAL	8	22	
CPK		82	mü/mī,	05/12/2000	NORMAL	0	120	
LDL.		50	MG/DL	05/12/2000	NORMAL	50	160	
SGPT	(ALT)	22	mU/mL	06/08/2000	NORMAL	5	25	
SGOT	(AST)	23 H	mU/mL	06/08/2000	INCREASED	8	22	•

	A.1. Patient Identi	fler		G.9. Mfr. n	sport number			
MED WATC	Н			200151	108724			
			<del></del>					
B.C. Balancant to the But								
B.6. Relevant tests/laboratory ( [continuation:]	data ,including dates							
CPK	86	mU/mL	06/08	3/2000	NORMAL	0	120	
TOTAL CHOLESTER	OL144	mg/dL	06/08	3/2000	NORMAL	125	200	
TRIGLYCERIDER (1	L173	mg/dL	06/08	/2000	NORMAL	45	200	
							•	
HDL (LIPIDS)	52	mg/dL	06/08	/2000	NORMAL	35	60	
÷								•
LDL (LIPIDS)	77	mg/dL	06/08	/2000	NORMAL	35	160	-
		***						2 =
SGPT (ALT)	32 H	mU/mL	08/31	/2000	INCREASED	5	25	
SGOT (AST)	30 H	mU/mL	08/31	/2000	INCREASED	8	22	
							••	
CPK	107	mU/mL	08/31,	/2000	NORMAL	0	120	
			,	,		V	120	
TOTAL CHOLESTERO	L150	MG/DL	08/31,	/2000	NORMAL	125	222	
			,,	2000	NORMAL	143	200	
TRIGLYCERIDER	69	MG/DL	08/31/	/2000	NORMAL	45		
	-	, 22	00,31,	2000	NORPALI	45	200	
HDL	57	MG/DL	09/21/	/2000	NORMAL	25	•	
		MG/ DL	06/31/	2000	NORMAL	35	60	
LDL	79	WG /P*	00/07	/aass				
	,	MG/DL	08/31/	2000	NORMAL	50	160	
CODING (append)	144							
SODIUM (SERUM)	144	MEQ/L	12/08/	2000		133	145	
DOM: 445								
POTASSIUM (SERUM	3.7	MEQ/L	12/08/	2000	NORMAL	3.5	5.0 ,	

	100	Patient Identifier	G.9. Mfr.	G.9. Mfr. report number					
MED WATC	H		20018	E08724				Page 10 of 13	
8.6. Relevant tests/laboratory		uding dates							
(concinuacion:)	CREATI	NINE (SERUM1.6 H	MG/I	DL 12/08	/2000	INCREASED	0.7	1.4	
TOTAL PROTEIN	8.7 H	GM/DL	12/08/2000	INCREASED	6.0	8.0			
CALCIUM	9.5	MG/DL	12/08/2000	NORMAL	8.5	10.5			
PHOSPHORUS	2.6	MG/DL	12/08/2000	NORMAL	2.5	4.5			
ALK PHOS >18	101 H	MU/ML	12/08/2000	INCREASED	32	72			
GAMMA GT	40 H	MU/ML	12/08/2000	INCREASED	5	29			7
TOTAL BILIRUBIN	2.33 В	MG/DL	12/08/2000	INCREASED	0.10	1.10			- -
SGPT (ALT)	59 H	. " MU/ML	12/08/2000	INCREASED	5	25			
SGOT (AST)	41 H	MU/ML	12/08/2000	INCREASED	8	22			
CPK	86	MU/ML	12/08/2000	NORMAL	0	120			
ALBUMIN	4.9	GM/DL	12/08/2000	NORMAL	3.5	5.5			
FP GLUCOSE	97	MG/DL	12/08/2000	NORMAL	60	115			
SGPT (ALT)	68 H -	MU/ML	02/15/2001	INCREASED	5	25			
SGOT (AST)	51 H	. MU/ML	02/15/2001	INCREASED	8	22			
CPK	93	MU/ML	02/15/2001	NORMAL	0	120			

77.7		ent Identifier	G.9. Mfr.	report number			
MED WAT	CH ¦		20015	E08724			
•							Page 11 of 13
8.6. Relevant testallaborator	y data , including	i dates					
[continuation:							
TOTAL CHOLESTE		MG/DL	02/35/2001	*****			
		2137 01	02/15/2001	. NORMAL	125	200	
TRIGLYCERIDES	85	MG/DL	02/35/000				
		265, 02	02/15/2001	. NORMAL	45	200	
HDL	46	MG/DL	00/15/000	****			
		287.00	02/15/2001	NORMAL	35	60	
LDL	70	MG/DL	00/15/000				1
	. •	MG/DL	02/15/2001	NORMAL	50	160	
SGPT (ALT)	33 H	367 /367					
,	33 <b>II</b>	MU/ML	05/09/2001	NORMAL	5	25	-
SGOT (AST)	27 н	MI /M	05/00/000				· ·
,	27 4	MU/ML	05/09/2001	INCREASED	8	22	
אר	113	1677 /100	***				
-	+13	· ~ MU/ML	05/09/2001	NORMAL	0	120	
TOTAL CHOLESTER	07.156	WG /D1	<b></b> ( (				
	02136	MG/DL	05/09/2001	NORMAL	125	200	
TRIGLYCERIDES	79	W0 /P*	<b>07</b> / <b>00</b> / <b>0</b> 000			•	
	,,	MG/DL	05/09/2001	NORMAL	45	200	
HDL	62 H	240 /					
	02 H	MG/DL	05/09/2001	INCREASED	35	60	
LDL	7.0						
	78	MG/DL	05/09/2001	NORMAL	50	160	
200m /hrm)							
SGPT (ALT)	29 H	MU/ML	08/01/2001	INCREASED	5	25	
GOT (AST)	25 H	MU/ML	08/01/2001	INCREASED	8	22	
		,					
PK	109	MU/ML	08/01/2001	NORMAL	0	120	
COTAL CHOLESTERO	L148	MG/DL	08/01/2001	NORMAL	125	200	•

			A.1. Pallent Identifi	1. Patient identifier		G.9. Mfr. report number					
1	MED WATC	Н				2001SE	08724			Page 12 of 13	
	8.6. Relevant tostalaboratory of [continuation:]	ista	.including dates								
	TRIGLYCERIDES	62		MG/DL	08/0	1/2001	NORMAL	45	200		
	HDL	62	H	MG/DL	08/01	L/2001	INCREASED	35	60		
	LDL	74		MG/DL	08/01	./2001	NORMAL	50	160		
i	24 HOUR URINE PR	0130	0	ИG							
	SODIUM	137		MMOL/L	Unkno	₩n					
1	POTASSIUM	3.9		MMOL/L	Unkno	WIL					
,	REA	5.5		MMOL/L	Unkno	wn					27
c	CREATININE	108		MMOL/L	Unkno	٧n					
A	ST	25									
A	LT	20									
c	PK	115									
н	В	13.7									
M	cv	82									
	cc	6.9	•								
1	•										

,	A.1. Patient identifier	G.S. Mir. report number	
MED WATCH		2001SE08724	
	I.		Page 13 of 13

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[continuation:] PLATELETS

360

ESR

CREATININE CLEARE57

ML/MIN

PROTEIN/CREATININ13.1

05/20/2002

EQUIVALENT TO 159 MG PROTEIN PER 24 HOUR.

PROTEIN/CREATININ16.4

05/27/2002

EQUIVALENT TO 110 MG PROTEIN PER 24 HOUR

C.18. Concordant medical products and therapy dates (exclude trestment of event)

[continuation:] Name: STEROIDS

"ame: BICILLIN Dates: 07/??/2001 to NI

G.3. Report source (other:)

Source

AstraZeneca Pharmaceuticals A Business Unit of AstraZeneca LP, 1800 Concord Pike, P.O. Box 15437, Wilmington, DE 19850-5437 Mfr. Rep. #: 2001SE08724

Date: 17-JUN-2002

LISTING OF PRIOR SAFETY REPORTS
SUBMITTED TO ....

ADVERSE EVENT: NEPHRITIS INTERSTITIAL

(all preferred and included coded terms)

Manufacturer Report # FDA Submission Date Protocol Number

2001SE08724 21-MAY-2002 4522IL/0034

**Country of Origin**